

Transforming mental health through psychoactive care pathways

Introductory overview

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Executive Summary

OPPORTUNITY

We address society's largest unmet medical need: depression

- ◇ Annual cost of depression of £300bn in EU and US alone
- ◇ Initial focus: treatment-resistant depression (TRD), representing 100m patients out of 320m globally
- ◇ Our vision is to accelerate patient access to evidenced-based innovation in mental health

A SOLUTION

We are developing psilocybin therapy as safe, superior TRD therapy

- ◇ Psilocybin therapy (with minimal supportive therapy) likely more efficacious, shorter in time, and at more affordable cost than alternatives for treatment-resistant depression
- ◇ Pivotal studies following current PhIIb trial could grant data exclusivity for 10-11 years in EU, an additional US-based trial could grant 5-7.5 years of data exclusivity in US

REASON TO BELIEVE

We work closely with top scientists, regulators, and technology players

- ◇ Actively engaged, highly respected advisors and partners from leading institutions
- ◇ European Medicines Agency (EMA) provides legal, regulatory, and scientific advice on clinical development plan

UNIT ECONOMICS

We will sell psilocybin therapy to healthcare delivery points, get reimbursed for outcomes

- ◇ Tech-supported psilocybin therapy sold with training and quality management
- ◇ Initial business model allows >50% contribution margin for COMPASS & clinics partners
- ◇ Additional upside based on outcome (value-based) reimbursement models

FINANCING

We raised £25m Series A in September 2018 for milestones to H2 2020 related to current Phase IIb

- ◇ Next 18 months: initial results of largest psilocybin clinical trial in history, preparation for Phase III pivotal trials, technology platform development
- ◇ Beyond: additional studies with psilocybin and other substances (early stage)

Patient Benefit: Patients who suffered from debilitating depression for 18 years finally found relief

“

With psilocybin, like Google Earth, you can zoom out. You're so used to being immersed in your day-to-day fog. It enables you to step back. On psilocybin, it was as if that concrete coat that you're constantly wearing day-to-day has been put to one side. You can see and feel things a lot more clearly. You're not immersed.

”

“

I had such instant relief I could make up my mind about things, what I want in terms of career, I had a clear mind, it lifted the fog of depression ... The way I felt after, I have not felt with any medicine or therapy or combination. I forgot what depression was – and I would even say to myself, ‘how could I be depressed or have this irrational thinking?’

”

Rethinking Psychiatric Care: COMPASS is addressing massive unmet medical need in mental health with psilocybin therapy



Note: <https://vimeo.com/232484518>

COMPASS IS DEDICATED TO ACCELERATING PATIENT ACCESS
TO EVIDENCE-BASED INNOVATION IN MENTAL HEALTH CARE

We will improve **mental health** through the development of new patient care pathways, based on advances in neuroscience, psychotherapy, psychopharmacology, and technology

Our first major initiative is developing **psilocybin therapy for patients with treatment-resistant depression** through late-stage clinical trials in the EU, US and Canada

Objective: COMPASS addresses depression, the largest and one of the fastest-growing health issues worldwide

Depression: leading cause of disability worldwide

- ✦ **320m people** suffering with depression, including 100m patients with treatment-resistant depression
- ✦ Single **most burdensome** illness (6%¹ global burden)
- ✦ Affected population **rose 18%** in 2005-2015



18%
INCREASE

Disease burden weighs on healthcare systems

- ✦ **Euro-28** annual cost of depression: **£140bn**
 - ✦ Direct costs²: £50bn (outpatient £27bn, inpatient £13bn, prescriptions³ £10bn)
- ✦ **US** annual cost of depression: **£160bn**
 - ✦ Direct costs: £75bn (outpatient £31bn, inpatient £14bn, prescriptions £30bn)

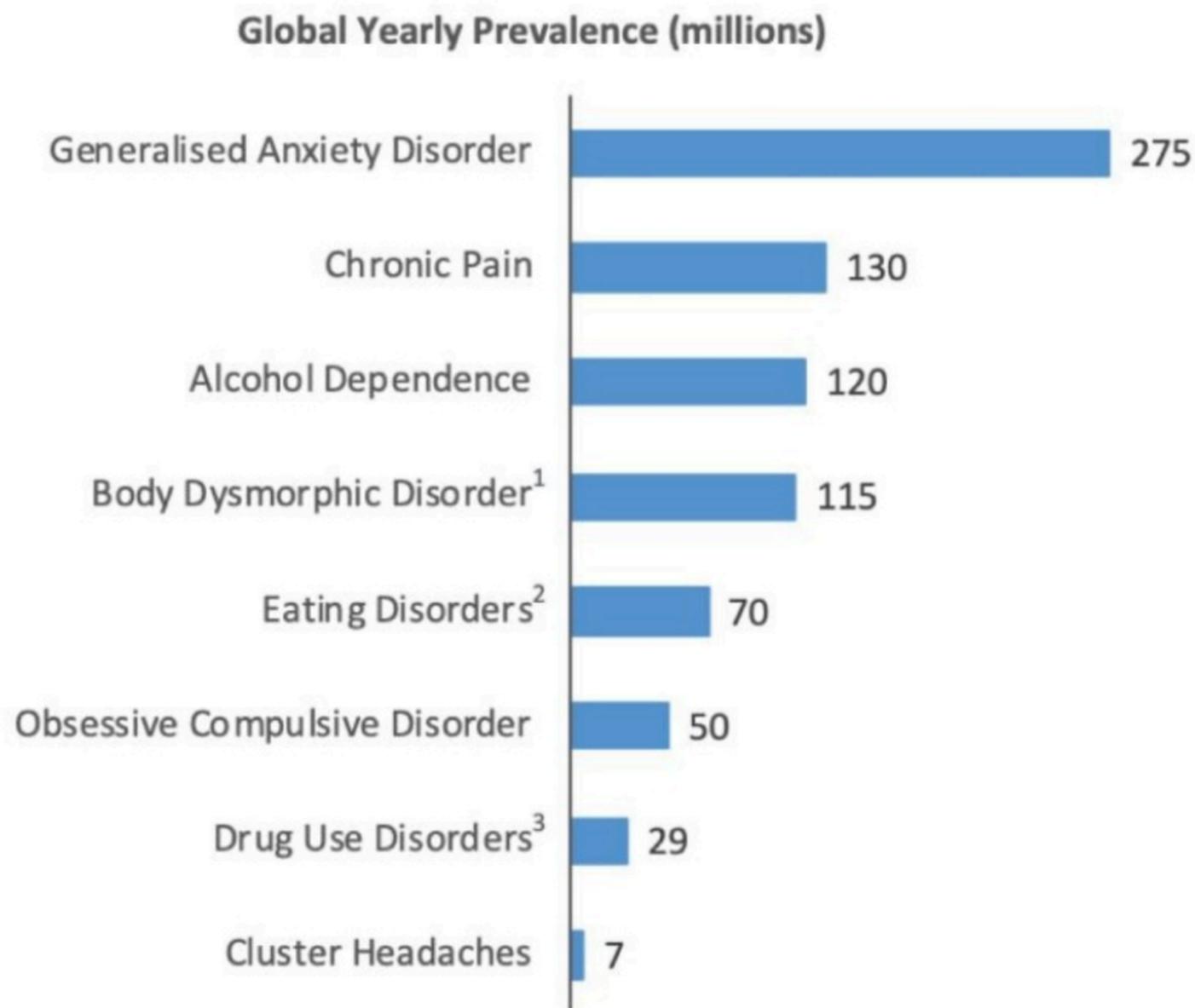


ANNUAL COSTS
EU+US

1. Disease burden measured in Disability-Adjusted Life Years (DALY) 2. Indirect costs include comorbidities, mortality, workplace productivity losses
3. SSRI/ SNRIs account for significant portion of drug costs

Objective: COMPASS aims to improve mental health across other disorders, which contribute to the suffering of hundreds of millions of people worldwide

Large number of people impacted by mental health problems ...



1. Includes sub-types Muscle Dysmorphia, Body Dysmorphic Disorder by Proxy 2. Includes Anorexia Nervosa, Bulimia, Binge Eating Disorder 3. Includes dependence to Opiates, Cocaine, Cannabis, Amphetamine-Type Stimulants, New Psychoactive Substances

... Resulting in significant suffering and costs globally

“

There is a collective failure to respond to this global health crisis, which results in monumental loss of human capabilities and avoidable suffering.

Estimates the rising cost will hit **\$16 trillion by 2030** (loss to the global economy of people of working age with mental health problems).

”

The Lancet Commission on Global Mental Health (2018)

Breakthrough Therapy: Psilocybin presents significant scientific and commercial opportunity

- ✓ **Value Proposition:** Attractive therapeutic, patient, and economic benefit profile, with over 70% of patients rank psilocybin therapy among top 5 most meaningful experiences of their lives¹
- ✓ **FDA 'Breakthrough Therapy Designation' received in Oct2018:** "Preliminary clinical evidence indicates the drug may demonstrate substantial improvement over existing therapies to treat a serious or life threatening disease or condition"
- ✓ **Promising clinical evidence:** Strong signals from Phase I/IIa studies by top research institutions in EU and US
- ✓ **Safe substance:** Low harm and dependence potential and no significant adverse events in studies
- ✓ **Strong IP position:** Never registered as new chemical entity (NCE) and strong protection from four independent sets of patent claims filed in UK/PCT*/US in Oct2018; market protection from generics for 8-11 years in EU, 5-7.5 years in US

* PCT = Patent Cooperation Treaty

Psilocybin Therapy: Attractive Value Proposition in terms of therapeutic, patient, and economic benefit

Value proposition: In patients with treatment resistant major depressive disorder (MDD), who have not responded to at least 2 courses of appropriately administered oral antidepressants, a short course of Psilocybin Therapy provides **greater and durable efficacy** on depressive symptoms, significant **improvement of functioning**, as well as **patient (and caregiver) health-related quality of life** and **reduced healthcare resource utilisation**.

Value claims: Compared to commonly prescribed oral antidepressant treatment regimens¹



PATIENT BENEFIT

- ✓ Faster and longer lasting relief from depressive symptoms
- ✓ Significant improvement in social, family, & occupational functioning and health-related quality of life (also for caregivers)
- ✓ Convenient experience, with no adherence concerns



THERAPEUTIC BENEFIT

- ✓ Superior efficacy
- ✓ More sustained/durable efficacy, ie longer remission/maintenance of response
- ✓ Safe and well tolerated, with no significant adverse event associated with commonly prescribed antidepressants or augmentation therapies



ECONOMIC BENEFIT

- ✓ More cost-effective, with reduced healthcare resource utilisation (HRU)
 - ✓ Lower hospitalisation rates
 - ✓ Fewer outpatient visits to GPs and psychiatrists
 - ✓ Delay/prevention of progression to more costly and invasive interventions)

1. Based on early-stage clinical studies and high level economic analysis

FDA 'Breakthrough Therapy' Designation: Award for psilocybin in TRD in October 2018 could mean faster access to patients

COMPASS received 'Breakthrough Therapy' designation (BTD) from US Food and Drug Administration (FDA) in Oct-2018 for its psilocybin therapy for treatment-resistant depression (TRD). This is a significant milestone for psilocybin therapy and psilocybin research, and a testament to the work done over many years by research teams in the US, the UK, and Switzerland.

'Breakthrough Designation' is awarded to investigative therapies with evidence demonstrating substantial improvement in serious or life-threatening condition

- ✧ Most are related to cancer (54%), followed by infectious disease (17%)
- ✧ In psychiatry, few therapies have recently received BTD, eg Esketamine (2013, 2016), Sage-217 (2018)

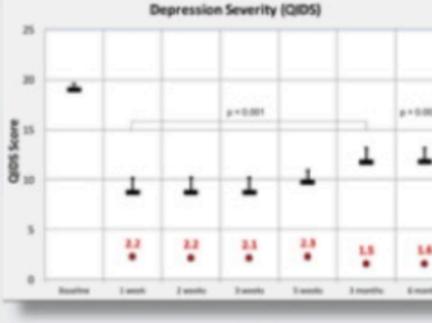
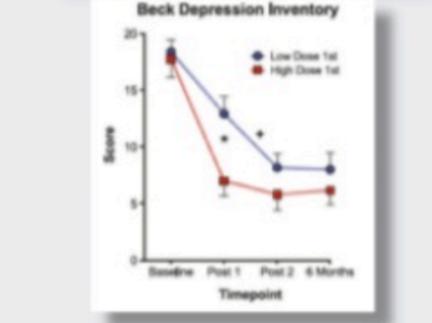
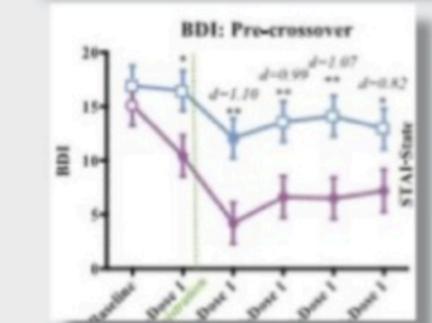
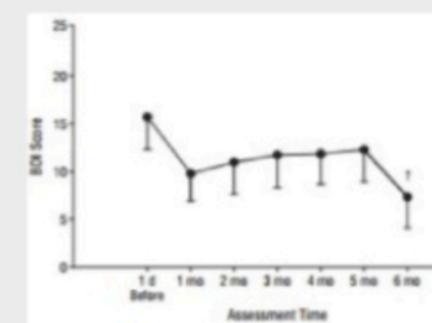
BTD is intended to accelerate approval of therapies and availability to patients

Clinical Programme Aspect		BTD	Non-BTD
Trial Programme	No. Pivotal Trials	1	2
	Total No. Subjects	222	446
Subjects	Double Blinding	46%	80%
	Randomisation	59%	89%
Comparators	Placebo/Active/Indirect	65%	87%
	None	35%	13%
Timelines	IND-to-Approval	4.9 years	12 years
	Submission-to-Approval	7 months	2 years
Fast Track ¹	Likelihood of Award	39%	12%

1. Fast Track award from FDA leads to more meetings and written communications with FDA for trial design and eligibility for Accelerated Approval award

Clinical Signals: Psilocybin therapy with immediate, significant, and sustained reduction in treatment-resistant depression & other illnesses

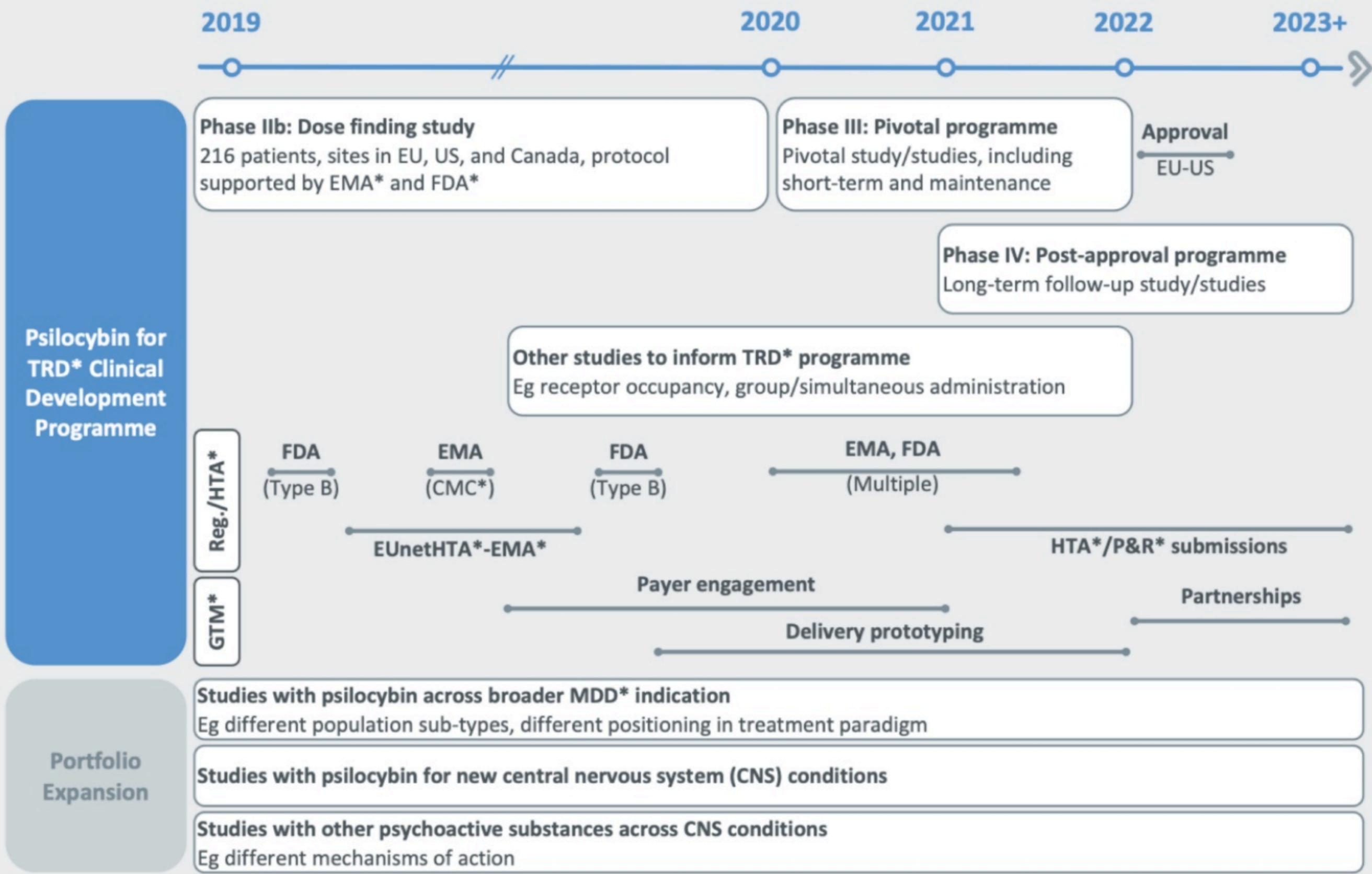
Trial	Key outcomes ¹
'11 U. California Los Angeles Grob et al	<p>Existential distress: Feasibility & safety for cancer patients</p> <ul style="list-style-type: none"> 12 patients, published in <i>Archives of General Psychiatry</i> BDI* showed significant improvement in mood (30%) at 6 months STAI* showed significant reduction in anxiety at 1, 3, and 6 months
'16 New York University Ross et al	<p>Existential distress: Immediate, substantial & sustained response</p> <ul style="list-style-type: none"> 29 patients, published in <i>Journal of Psychopharmacology</i> BDI* showed significant improvement at 2 and 8 months Anti-depressant response rates: between 60-80% at 6 months
'16 John Hopkins Griffiths et al	<p>Existential distress: Substantial & sustained response</p> <ul style="list-style-type: none"> 51 patients, published in <i>Journal of Psychopharmacology</i> BDI* showed significant improvement at 1, 3, 6 months Anti-depressant response rates: 92% at 5 weeks, 79% at 6 months
'16 Imperial College London Carhart-Harris et al	<p>TRD: Preliminary support for safety & efficacy</p> <ul style="list-style-type: none"> 12 patients, published in <i>The Lancet</i> (additional 7 patients in press) Median of 4 failed treatments, mean duration of illness of 18 years BDI/QIDS* significant improvement ($p < 0.001$) at 1, 3², 5, 12² weeks 63% of patients with response at 1 week, 47% at 5 weeks, 32% no further medication or therapy at 1 year



Positive signals from early-stage trials present commercial opportunity for treatment-resistant depression, according to health care regulators

* BDI = Beck Depression Inventory; QIDS = Quick Inventory of Depressive Symptoms; STAI = State-Trait Anxiety Inventory
 1. Detailed outcomes in scientific package 2. Based on data from 12 patients (different end points measured)

Approach: High level timeline for psilocybin in TRD Regulatory approval, Market Access and HTA appraisals, and related development activities



* CMC = Chemistry, Manufacturing, and Controls; EMA = European Medicines Agency; EUnetHTA = European network of HTA agencies; FDA = Food & Drug Administration; GTM = Go-To-Market; HTA = Health Technology Assessment; MDD = Major Depressive Disorder; P&R = Pricing & Reimbursement; TRD = Treatment-Resistant Depression